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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/124,485	07/29/1998	NICHOLAS MARK ANSTEY	73-97	6763

7590

06/02/2003

GREENLEE WINNER AND SULLIVAN
5370 MANHATTAN CIRCLE
SUITE 201
BOULDER, CO 80303

EXAMINER

CHEU, CHANGHWA J

ART UNIT

PAPER NUMBER

1641

DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/124,485

Applicant(s)

ANSTEY ET AL.

Examiner

Jacob Cheu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 January 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 27-33, 38-43 and 45-47 is/are pending in the application.
- 4a) Of the above claim(s) 27-33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38-43, 45-47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

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DETAILED ACTION

Applicant's amendment filed on January 9, 2003 has been received, entered into record and considered. The following information provided in the amendment affects the instant application:

1. Claim 44 is cancelled without prejudice.
2. Claims 46 and 47 are added to the instant application.
3. Remarks drawn to the rejection of claims 38-39, 42-43 and 45 under 35 U.S.C 103 (a).

Response to Amendment

Claim Rejections - 35 USC § 112

1. Claims 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 41, line 2, "nitric oxide effect" is vague and indefinite. It is unclear what nitric oxide "effect" applicant refers to.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. Claims 38-43, 46-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kremsner et al (Transactions Royal Society Medicine Hygiene (1996) 90: 44-47) in view of Green (USP 5814666).

Kremsner et al. teach that nitric oxide (NO) plays a key role in protective of infectious disease, i.e. malaria, in non-rodent mammal, i.e., children, caused by *Plasmodium falciparum* (Abstract and first paragraph, page 47) However, Kremsner et al. do not specifically teach administering a NO releasing agent through inhalation to kill, inhibit or retard the parasite in treating the related disease. Green et al. teach a generic method in combating infectious disease, e.g. parasite, bacteria, or virus, by administering NO releasing agents through inhalation to inhibit or kill the microorganisms. (Col. 13, line 40-50; Table I, claims 1 and 12) Green et al. also teach that the transferring moiety could be selected from biopolymers including, peptides, proteins, nucleic acids, antibodies and the like. (Col. 10, line 12-15) Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have provided Kremsner et al. with the NO releasing agents and the method of administering NO agents taught by Green et al. since combating the parasite infectious disease, i.e. *Plasmodium falciparum* malaria has been attributed to NO's protective role and the NO releasing agents are readily known and available at the time the invention was made.

5. Claims 38-44, 46-47 rejected under 35 U.S.C. 103(a) as being unpatentable over Anstey (J. Exp. Med. (1996) 184: 557-567) et al. in view of Green.

Anstey et al. teach that nitric oxide (NO) plays a key role in suppression of a human pathogen, i.e. *Plasmodium falciparum*, in reducing the severity of the malaria disease.

(Abstract and first paragraph, page 564, last paragraph) Similarly, Anstey et al. do not specifically teach administering a NO releasing agent through inhalation to kill, inhibit or retard the parasite in treating the related disease. Nevertheless, the deficiency of Anstey et al. can be cured by the reference of Green as discussed above. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have provided Anstey et al. with the NO releasing agents and the method of administering NO agents taught by Green et al. since combating the parasite infectious disease, i.e. *Plasmodium falciparum* malaria has been attributed to NO's protective role and the NO releasing agents are readily known and available at the time the invention was made.

6. Claim 45 is rejected under 35 U.S.C. 103 (a) as being unpatentable over Kremsner et al. or Anstey et al. in view of Green et al., as applied to claims 38-43, further in view of Weinberg. (Blood (1995) 86: 1184-1195)

Both Kremsner and Anstey et al. references have been discussed supra but fail to teach specifically the NO releasing agents as in the recited group in the instant claim. Weinberg et al. teach that several agents participating activating the NO production, including lipopolysaccharide (LPS), cytokines, IFN γ , TNF, IL-1, INF γ . (See Introduction, page 1184, first paragraph) Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided either Kremsner or Anstey et al in combination with Green et al. with the NO releasing agents taught by Weinberg et al. to treat the patients of *Plasmodium falciparum* malaria disease since it is well known in the art that these agents can increase the production of NO in the biological system. Supra.

Response to Arguments

6. Applicant's arguments with respect to claim 38-44, 46-47 have been considered but are moot in view of the new ground(s) of rejection set forth in this Office Action.

With respect to the reference of Green et al., applicant argues that there exists discrepancy between the instant invention and the teachings of Green et al., i.e. different parasites, namely *Plasmodium* and *Leishmania*. The argument is considered but is not persuaded. Because Green et al. teach that NO releasing agents have a therapeutic value in treating with infectious disease, albeit not specifically related to *Plasmodium* malaria. Nonetheless, the scope of the instant invention falls within the scope of the reference of Green et al. because treatment of infectious disease is a common concern in medicine. Second, the findings of Kremsner et al. and Anstey et al, i.e. NO plays a protective role in the malaria disease, would be a suggestion or motivation to one skilled in the art to use the NO releasing agents taught by Green et al. to combat the specific disease caused by *Plasmodium* with a reasonable expectation of success. Because (1) Green et al. teach administering NO releasing agents to human which is the same subject tested in both Kremsner and Anstey et al. references; (2) NO releasing agents can cause more production of NO in a biological system which is needed in both Kremsner and Anstey et al. references; (3) the similar results to produce more NO, as far as *not too excessive* suggested by Kremsner et al, is useful in combating the infectious disease of interest.

With respect to the reference of Kremsner et al., although there might be two factors overlooked by Kremsner et al, namely dietary restriction and renal impairment (See Anstey et al. Correspondence on Trans. Royal. Tropic Med. Hyge. (1997) 91: 238-240; Last paragraph), Kremsner et al. still explicitly teach, even citing other investigators' findings, that NO plays a *protective role* in combating the disease. (See Discussion, page 46, right column) Applicant's argument that the reference of Kremsner et al. presents an opposite review, i.e. causative role of NO, serving as a suggestion teaches away one having ordinary skill in the art from using NO as a cure agent for the infectious disease. The Examiner does not agree with this interpretation because Kremsner et al. do not explicitly teach that NO is a caustic factor in malaria disease. Rather Kremsner et al. suggest that the excessive level of NO may be deleterious (See Discussion, last line in page 46, right column), therefore such level, i.e. excessive level, of NO may play a causative role in the severe malaria. (See the middle right portion of the discussion *supra*)

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Most importantly, Kremsner et al. indicates that "*NO produced within the network of a directed immune response may overall play a key protective role*". (Emphasis added, See Discussion, page 47, first paragraph) In the absence of an effective range of the NO recited by the applicant, the concept of administering a NO releasing agents to generate NO in combating infectious disease caused by *Plasmodium* is not novel but known to ordinary skilled in the art such as Kremsner et al.

Conclusion

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 703-306-4086. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-305-3399.

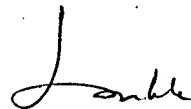
Jacob Cheu

Examiner

Art Unit 1641



May 30, 2003



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SUPERVISORY PATENT EXAMINER
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05/30/03